

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings of claims in the application:

LISTING OF CLAIMS:

1-54. (cancelled)

55. (currently amended) A genetically modified ~~rodent~~ all of whose cells comprise a mouse having its genomic Serca ATPase gene modified by inserted recombination sites, [[the]] of heterogeneous origin, said modification being homozygous.

56. (currently amended) The ~~rodent~~ mouse of claim 55 comprising several copies of the modified Serca ATPase gene.

57. (currently amended) The ~~rodent~~ mouse of claim 55, wherein the Serca ATPase gene is a Serca2 ATPase gene.

58. (canceled)

59. (currently amended) The ~~rodent~~ mouse of claim [[58]] 55, wherein the heterogenous recombination sites are of non-mammalian origin.

60. (currently amended) The ~~rodent~~ mouse of claim [[59]] 55, wherein the recombination sites comprise loxP recombination sites.

61. (currently amended) The ~~rodent~~ mouse of claim 55, ~~all of whose cells further comprise~~ comprising a gene encoding a heterogenous recombinase.

62. (currently amended) The ~~rodent~~ mouse of claim 61, wherein the heterogenous recombinase is of non-mammalian origin.

63. (currently amended) The ~~rodent~~ mouse of claim [[62]] 61, wherein the recombinase is a Cre recombinase.

64. (currently amended) The ~~rodent~~ mouse of claim 61, wherein expression of the recombinase encoding gene is controlled by a regulatory nucleic acid sequence.

65. (currently amended) The ~~rodent~~ mouse of claim 64, wherein the regulatory nucleic acid sequence is inducible.

66. (currently amended) The ~~rodent~~ mouse of claim [[65]] 64, wherein said regulatory nucleic acid sequence is inducible by tamoxifen.

67. (currently amended) The ~~rodent~~ mouse of claim 61, wherein expression of the recombinase gene is tissue-specific.

68. (currently amended) The ~~rodent~~ mouse of claim 67, wherein expression of the recombinase gene occurs in heart tissue.

69. (canceled)

70. (currently amended) [[A]] An eukaryotic cell,
~~comprising a Serca ATPase gene modified by inserted recombination~~
~~sites, the modification being homozygous~~ having its genomic Serca
ATPase gene modified by inserted recombination sites of
heterogeneous origin, said modification being homozygous.

71. (currently amended) The cell of claim 70, comprising
several copies of the modified Serca ATPase gene.

72. (previously presented) The cell of claim 70, wherein
the Serca ATPase gene is a Serca2 ATPase gene.

73. (canceled)

74. (previously presented) The cell of claim 70, wherein
the heterogenous recombination sites are of non-mammalian origin.

75. (currently amended) The cell of claim ~~[[740]]~~ 70, wherein the recombination sites comprise loxP recombination sites.

76. (currently amended) The cell of claim 70, further comprising a gene encoding a heterogenous recombinase.

77. (previously presented) The cell of claim 76, wherein the heterogenous recombinase is of non-mammalian origin.

78. (currently amended) The cell of claim ~~[[77]]~~ 76, wherein the recombinase is a Cre recombinase.

79. (previously presented) The cell of claim 76, wherein expression of the recombinase encoding gene is controlled by a regulatory nucleic acid sequence.

80. (previously presented) The cell of claim 79, wherein the regulatory nucleic acid sequence is inducible.

81. (previously presented) The cell of claim 70, wherein the cell is of mammalian origin.

82. (currently amended) The cell of claim [[81]] 70, wherein the cell is of non-human mammalian origin.

83. (currently amended) The cell of claim [[82]] 70, wherein the cell is of rodent origin.

84. (currently amended) The cell of claim [[83]] 70, wherein the cell is of mouse origin.

85. (previously presented) The cell of claim 70, wherein said cell is an embryonic cell.

86. (previously presented) The cell of claim 70, wherein said cell is a cardiomyocyte.

87. (currently amended) A gene encoding a Serca ATPase modified by inserted recombination sites, wherein said recombination sites are heterogenous to said gene.

88. (currently amended) The gene of claim 87, wherein the Serca ATPase is a Serca2 ATPase.

89. (canceled)

90. (currently amended) The gene of claim [[89]] 87, wherein the heterogenous recombination sites are of non-mammalian origin.

91. (currently amended) The gene of claim [[90]] 87, wherein the recombination sites comprise loxP recombination sites.

92. (currently amended) The gene of claim [[88]] 87, wherein said gene is ~~substantially~~ modified as set forth in ~~SEQ ID 1~~ at least one of SEQ ID NO: 1-3.

93. (currently amended) A vector comprising the gene of claim [[33]] 87.

94. (previously presented) The vector of claim 93, wherein the vector is based on pBluescript II KS.

95-101. (canceled)

102. (currently amended) A method for screening a compound or a mixture of compounds for activity against defective Ca^{2+} handling, comprising the ~~steps of inducing recombination and inactivation of a Serca ATPase gene in a non human vertebrate;~~

~~administering the compound or mixture to said mammal before and/or after the induced inactivation of the Serca ATPase gene~~
following steps:

- inducing expression of the recombinase, and with that inactivation of the Serca ATPase gene, in the mouse according to claim 55;

- administering the compound or a mixture of compounds to said mouse before and/or after the induced inactivation of the SercaATPase gene; and

- detecting whether the induced defective CA^{2+} handling is normalized by the administration of said compound or mixture of compounds.

103. (previously presented) The method of claim 102 wherein the Serca ATPase gene is a Serca2 ATPase gene.

104. (currently amended) The method of claim 102, wherein ~~the Serca gene is inactivated~~ expression of the recombinase gene occurs in heart tissue.

105. - 108. (cancelled)

109. (new) The method of claim 102, wherein said method is suitable for screening a compound or a mixture of compounds for activity against heart failure.